IL 10-98-013
In Reply Refer To: 11

June 11, 1998

UNDER SECRETARY FOR HEALTH'S INFORMATION LETTER

HEPATITIS C: STANDARDS FOR PROVIDER EVALUATION AND TESTING

1. **Background:** Hepatitis C virus (HCV) infection was first recognized in the 1970's, when the majority of transfusion-associated infections were found to be unrelated to hepatitis A and B, the two hepatitis viruses recognized at the time. This transmissible disease was then simply called "non-A, non-B" hepatitis. Sequencing of the HCV genome was accomplished in 1989, and the term hepatitis C was subsequently applied to infection with this single strand ribonucleic acid (RNA) virus. The genome of HCV is highly heterogeneous and, thus, the virus has the capacity to escape the immune surveillance of the host; this circumstance leads to a high rate of chronic infection and lack of immunity to reinfection. Reliable and accurate (second generation) tests to detect antibody to HCV were not available until 1992, at which time an effective screening of donated blood for HCV antibody was initiated.

2. HCV infection is now recognized as a serious national problem. Nearly 4 million Americans are believed to be infected, and approximately 30,000 new infections occur annually. Only about 25 to 30 percent of these infections will be diagnosed. HCV is now known to be responsible for 8,000 to 10,000 deaths annually, and this number is expected to triple in the next 10 to 20 years.

3. Hepatitis C has particular import for the Department of Veterans Affairs (VA) because of its prevalence in VA's service population. For example, a 6-week inpatient survey at the VA Medical Center, Washington, DC, revealed a prevalence of 20 percent antibody positivity. A similar investigation at the VA Medical Center San Francisco, CA, found 10 percent of inpatients to be antibody positive. Veterans Health Administration (VHA) Transplant Program data reveal that 52 percent of all VA liver transplant patients have hepatitis C. An electronic survey of 125 VA medical centers conducted by the Infectious Disease Program Office from February through December of 1997, identified 14,958 VA patients who tested positive for hepatitis C antibody. Clearly, HCV infection is becoming a leading cause of cirrhosis, liver failure, and hepatocellular carcinoma. The incidence and prevalence rates are higher among nonwhite racial and ethnic groups.

4. HCV is transmitted primarily by the parenteral route. Sources of infection include transfusion of blood or blood products prior to 1992, injection drug use, nasal cocaine, needlestick accidents, and, possibly, tattooing. Sexual transmission is possible, and while the risk is low in a mutually monogamous relationship, persons having multiple sexual partners are at higher risk of infection.

5. After infection, 90 percent of HCV infected patients will develop viral antibodies within 3 months. The disease becomes chronic in 85 percent of those infected, although one-third will have normal aminotransferase levels. The rate of progression is variable, and chronic HCV infection leads to cirrhosis in at least 20 percent of infected persons within 20 years; 1 to 5 percent of those infected will develop hepatocellular carcinoma.

6. At present, treatment for HCV infection is limited, consisting primarily of administration of interferon alpha, with or without the addition of ribavirin. The treatment benefits some patients and appears to alter the natural progression of the disease, although evidence is lacking that it will translate into improvements in quality of life or reduction in the risk of hepatic failure. Current regimens include the use of 6 or 12-month courses of interferon alpha, with or without ribavirin. The recent National Institutes of Health Consensus Statement on Hepatitis C concluded that liver biopsy should be performed prior to initiating treatment. If little liver damage is apparent, therapy need not be initiated; treatment is probably appropriate for those with significant histologic abnormalities. However, data presented at this Consensus Conference indicated that significant uncertainty remains regarding indications for treatment. Treatment options and a listing of VA protocols will be the subject of a separate Information Letter.

7. A number of serologic tests are available for diagnosis and evaluation of HCV infection. Enzyme immunoassays (EIA) are "first line" tests, and are relatively inexpensive. They contain HCV antigens and detect the presence of antibodies to those antigens. Recombinant immunoblot assays (RIBA) contain antigens in an immunoblot format, and are used as supplemental or confirmatory tests. Viral RNA can be detected by reverse-transcription polymerase chain reaction (PCR) testing. Quantitative HCV RNA testing uses target amplification PCR or signal amplification (branched deoxyribonucleic acid (DNA)) techniques.

8. The EIA tests have sensitivities in the range of 92 to 95 percent. Specificities depend on the risk stratification pre-testing. That is, in blood donors with no risk factors, 25 to 60 percent of positive EIA are also positive by PCR for viral RNA. About 75 percent of low risk donors with positive EIA and RIBA will be positive by PCR. Positive EIA tests should be confirmed by RIBA. If that is also positive the patient has, or has had, HCV infection. In high-risk patients who are EIA positive, particularly if there is evidence of liver disease, supplemental testing with RIBA or HCV RNA analysis is probably unnecessary. Quantitative RNA tests may be useful in the selection and monitoring of patients undergoing treatment.

9. All patients will be evaluated with respect to risk factors for hepatitis C, and this assessment documented in the patient's chart. Based upon those risk factors, antibody testing should be utilized as elaborated on in the algorithm found in Attachment A.

S/Kenneth W. Kizer, M.D., M.P.H.
Under Secretary for Health

Attachment

DISTRIBUTION: CO: E-mailed 6/11/98
FLD: VISN, MA, DO, OC, OCRO, and 200 – FAX 6/11/98
EX: Boxes 104,88,63,60,54,52,47,and 44 – FAX 6/11/98

ATTACHMENT A

HEPATITIS C VIRUS ANTIBODY SCREEENING FOR THE VETERAN POPULATION